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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

BORIN, MICHAEL L

ART UNIT

PAPER NUMBER

1631

MAIL DATE

DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/523,131	Applicant(s) OFER, DROR	
	Examiner Michael Borin	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 February 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,10-12,16-25,28-31,33,36,38-41 and 78-87 is/are pending in the application.
- 4a) Of the above claim(s) 7,10-13,16-23,37-39,50-53,57,102 and 103 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6,8,9,14,15,24-36,40-49,54-56,155,156 and 158-163 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>04/13/2006</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Claims

Claims 58-101, 104-154, 164-171 are canceled. Claims 1,2,10-12,16-25,28-31,33,36,38-41,78-87 are pending.

Response to restriction and election of species requirements are acknowledged. Applicant elected, without traverse, Group I, claims 1-6, 8, 9, 14-18, 21-57, 102, 103, 155-163 and canceled claims 164-171 directed to Group II.

Further, pursuant to election of species, claims 7,10-13,16-23,37-39,50-53,57,102,103,157 are withdrawn as being drawn to a non-elected species. Please note that claim 8, indicated by applicant as being withdrawn remains under consideration as being a base claim for claim 9 (elected species). Conversely, claim 20 is withdrawn from consideration as being dependent on withdrawn claim 19. Please correct claim identifiers for these claims.

Claims 1-6,8,9,14,15,24-36,40-49,54-56,155,156,158-163 are under examination.

Information Disclosure Statement

Applicants' Information Disclosure Statement filed 04/13/2006 has been received and entered into the application. Accordingly, as reflected by the attached completed copies of forms PTO-1449, the cited references have been considered.

Claim Objections

Claims 34,35 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. The claims are directed to use of more than one set of gauges whereas the base claim 1 is directed to use of one set of gauges. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim Rejections - 35 USC § 112, second paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6,8,9,14,15,24-36,40-49,54-56,155,156,158-163 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and

distinctly claim the subject matter which applicant regards as the invention. Claim 1 is amended to recite that The rejection is applied for the following reasons.

A. Claim 1: The term “mathematical-chemical space” is vague and indefinite. The term is not defined either by the claim or by specification. Specification addresses “measurement space ([0067]), “virtual space” ([0110]), “space of models” ([0038]), “array of spaces, one space for each set of chemical behaviors “ ([0138]), “chemical configuration space”([0162]), but does not address “mathematical-chemical space”. Therefore, one of ordinary skills in the art would not be reasonably appraised of the scope of the invention.

B. Claim 1: The claim addresses “chemical gauges” which are understood as molecules. The claim then follows to address “geometric substructures” of the gauges. A molecule does not have geometric, triangular or otherwise, substructures. At best a model, geometric, virtual, etc., may be addressed as having “geometric substructures”. Please clarify via clearer claim language.

C. Claim 1: A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by “such as” and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely

exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 1 recites the broad recitation that only at least 50% of mathematical-chemical space is spanned by triangular substructures, and the claim also recites that each point in space is covered by at least 5 distinct gauges which is the narrower statement of the range/limitation.

is amended to address various “masses”, such as “associated mass”, “corresponding mass”. Further, the claim is directed to indices which are “representing” an “associated mass”.

The terms “associated” and “corresponding” are vague and indefinite; it is not clear what is encompassed by such definitions and what is the difference between them.

Further, the meaning “representing” an “associated mass”. is also indefinite. What does it mean to “represent an “associated mass”. Clarification via clearer language is requested.

D. Claim 1: The phrase “each point in space” is not clear. The term “point” with regard to the “mathematical-chemical space” is vague and unclear; it does not define the scope of what is being “covered by at least 5 distinct gauges” and one of ordinary skills in the art would not be reasonably appraised of the scope of the invention. The answer is essential to define what is supposed to be covered by gauges as claimed.

E. Claim 1: It is not clear whether the claimed invention is directed to *in silico* method, *in vitro* method, or combination of the two. The claims address both “mathematical-chemical space” and “causing and assaying interactions”, which might be understood as directed to *in silico* and *in vitro* method steps. Specification address assaying of both in *in silico* (see paragraphs [0110],[0111],[0463] for example) and in *in vitro* conditions (see paragraph [0588], for example. Please clarify via clearer claim language.

F. Claims 29-31, 44-46,161: With regard to claims addressing “binding”, it is not clear whether the binding refers to binding in the course of , presumably *in vitro*, interaction of gauges with the target, or to binding in the sense of descriptor of a gauge’s ability to interact in “mathematically-chemical space”, i.e., presumably, *in silico*.

G. Claims 24,25,27, 28,44-46,160-162: With regard to claims addressing plurality of gauges, it is not clear whether the gauges in the set are all of distinct structure .

H. Claims 27,28,160,161: The same ambiguity with regard to the term “point” applies to claims 27,28,160,161. Further, it is not clear whether the term “point” of “mathematical-chemical space” in claim 1 has the same meaning as “point” in “virtual space” in claims 27,28,160,161. Please clarify via clearer claim language.

Further, with regard to claims 27,28, the term “substantially” is vague and indefinite: it is not clear what is being covered by “at least two gauges”

I. Claim 8: The claim addresses the result of identifying configuration that does not match a configuration of a bound gauge. It is not clear how, in the absence of further defining of the area to be assayed, one can know that there will be configurations that do not match a configuration of a bound gauge.

J. Claims 14,15: The claims address the result of covering certain number of chemical binding areas (four – in claim 14, six – in claim 15). Similarly to claim 8, above, it is not clear how, in the absence of further defining of the area to be assayed, one can know of amount of areas to be discovered by the method prior to applying the method itself

K. Claims 29-31: The claims address the amount of gauges that bind with the target. Similarly to claim 8, above, it is not clear how, in the absence of further defining of the area to be assayed, one can know of amount of amount of gauges that bind with the target to be discovered by the method prior to applying the method itself.

L. Claims 47-49: The claims are directed to identifying certain amount of different configurations. Similarly to claim 8, above, it is not clear how, in the absence of further defining of the area to be assayed, one can know of amount of different configurations to be discovered by the method prior to applying the method itself.

M. Claim 26: The claim addresses that gauges “comprise moieties arranged in spatial configurations” . It is not clear whether “spatial configurations of moieties” differ from the spatial orientation of gauges which themselves are defined as having rigid

geometrical substructure. See for example, one embodiment addressed in paragraph [0032] discussing that “the geometrical sub-structure may be three moieties arranged in a triangle”

N. Claim 34: The phrase “at least said set of gauges” makes unclear how many sets are being used. The base claim 1 is directed to just one set of gauges.

O. Claim 43: The meaning of the term “control area” is not clear. The specification, although providing particular examples (paragraph , does not provide a standard for ascertaining the requisite composition, and one of ordinary skills in the art would not be reasonably appraised of the scope of the invention.

Claim Rejections - 35 U.S.C. § 101

The following is a quotation of the 35 U.S.C. § 101:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 1-6,8,9,14,15,24-35,40-49,54-56,155,156,158-163 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

As it is unclear whether the claimed method is purely computational or *in vitro*, or combination of the two - see rejection (E) under 112, second paragraph, above, – and assuming that the method is computational, the following rejection applies.

The instant claims are drawn to a computer process of aligning query protein sequence with protein structures. The method includes computational steps of

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selecting functions and constraints, and performing linear programming analysis. The claims do not recite any practical application of the method.

To be statutory, an invention must be directed to one of statutory categories enumerated in 35 USC § 101, or must produce a result which is useful, and tangible, and concrete. In determining if the instant claims are useful, tangible, and concrete, the Examiner must determine each standard individually. For a claim to be “useful,” the claim must produce a result that is specific, substantial, and credible. For a claim to be “tangible,” the claim must set forth a practical application of the invention that produces a real-world result. For a claim to be “concrete,” the process must have a result that can be substantially repeatable or the process must substantially produce the same result again. Furthermore, the claim must recite a useful, tangible, and concrete result in the claim itself.

In addition, a claim must be limited only to statutory embodiments. Thus, if the claim is broader than the statutory embodiments of the claim, the Examiner must reject the claim as non-statutory.

The instant claims do not include any tangible result. A tangible requirement requires that the claim must set forth a practical application of the computational steps to produce a real-world result. No practical result is recited in the claims; thus the instant claims do not include any tangible result.

Claim Rejections - 35 U.S.C. § 101/ 112-1

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6,8,9,14,15,24-36,40-49,54-56,155,156,158-163 are rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility due to its not being supported by either specific and/or substantial utility or a well established utility.

As it is unclear whether the claimed method is purely computational or *in vitro*, or combination of the two - see rejection (E) under 112, second paragraph, above, – and assuming that the method is *in vitro* experimental, the following rejection applies.

Claims 1-6,8,9,14,15,24-36,40-49,54-56,155,156,158-163 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for use of small sets of gauges , does not reasonably provide enablement for use of sets of indefinitely large amount of gauges (e.g., thousands, as in claims 24,25). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claimed method is directed to use of simultaneous amount of a set of gauges to interact with the target molecule and evaluate its “chemical active area” .

Specification teaches that a screening library may be “comprising a set of at least 10,000 substantially rigid molecules. Optionally, said set comprises at least 50,000 substantially rigid molecules. Alternatively or additionally, said set comprises at least 100,000 substantially rigid molecules.” Paragraph [0203]. Specification describes theoretical use of such plurality of gauges (e.g., paragraph [0402]), but, apart from mentioning that high throughput systems are available (paragraph [0353]), and that methods such as NMR binding assay or an x-ray crystallography can be used (paragraph [0355]), does not teach how to use a large plurality, e.g., 100,000 gauges interacting at the same time with the target molecule.

Fejzo et al. (The SHAPES strategy: an NMR-based approach for lead generation in drug discovery . Chemistry & Biology , Volume 6 , Issue 10 , Pages 755 – 769, 2000) teaches that using mixtures of large amounts of compounds (gauges) simultaneously to analyze target molecule is problematic

Several problems could arise in screening mixtures of compounds. For example, any single compound with a ten- or hundred-fold higher binding affinity than others in the mixture would compete successfully for most protein binding sites, particularly if ligands are present in excess, and therefore one or more potential binders might be missed. This problem is important because simple modifications to a weak binding scaffold might result in enormous increases in binding affinity at later design stages, so missing potential scaffolds early in the screening process might eliminate an entire compound class from further development.

Another problem with using mixtures is spectral overlap. If overlap is severe, analysis of 1D spectra might not be possible, and analysis of 2D spectra would be difficult.

Specification, while addressing use of experimental methods, such as NMR (paragraph [0355]), for example), does not offer guidance on how to resolve the technical issues of using sets of indefinitely large amount of gauges.

In view of the above, it is the Examiners position that with the insufficient guidance and working examples and in view of unpredictability and the state of art one skilled in the art could not make and/or use the invention with the claimed breadth without an undue amount of experimentation.

Claim Rejections - 35 USC § 102 and 103.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

In view of ambiguity of the base claim 1 (see rejections of claim 1, and claims dependent thereupon, under 35 U.S.C 112, second paragraph above), it was not possible to carry out the search of prior art addressing all the limitations of the gauges as claimed. Generally, any reference addressing assaying interaction of a target molecule with a plurality of test molecules, the latter comprising a “rigid” chemical structure, would read on the invention as claimed (without the limitations describing the “gauges” themselves). Therefore, the Examiner applied an exemplary general rejection reading the broad scope of the claims as directed to method of obtaining information about a chemically active area of a target molecule, comprising providing a set of substantially rigid chemical gauges; causing said target to interact with a plurality of gauges; assaying said interaction of said gauges with said target, and analyzing said assay results to obtain information about said chemically active area.

Claims 1-4,26,29,29-33,36,41-46,155,156,158,159,161 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C.103(a) as obvious over Fejzo et al. (The SHAPES strategy: an NMR-based approach for lead generation in drug discovery . Chemistry & Biology , Volume 6 , Issue 10 , Pages 755 – 769, 2000; see IDS).

Fejzo et al. teach method of obtaining information about a chemically active area of a target molecule, comprising

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- providing a set of diverse library of small molecules. See Fig 1, for example. The molecules therein are all substantially rigid structures as they all have aromatic rings. The latter aromatic moieties all comprise what is addressed in the instant claims as “substantially rigid triangular geometric substructure, because any 6-member ring can be envisioned as comprising “triangular substructures of binding points” - e.g., triangular substructure connecting positions 1,3 and 5 of a 6-member ring. Further, the reference teaches that the compound scaffolds are derived from the shapes commonly found in known therapeutic agents (Abstract and p. 756, right column.
- assaying said interaction of said gauges with said target . See p. 759-762.
- analyzing said assay results to obtain information about said chemically active area. See p. 759-763.

Further, with respect to claim 26, the reference teaches juxtaposition of side chains and scaffolds. See p. 256, right column, first full paragraph.

Further, with respect to claims 41-43 , the reference describes proteins used. See p. 756, second full paragraph; p. 761, left column)

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Further, with respect to claims 32,33, the reference teaches at least 41 scaffold with 30 most common side chains. see p. 756, right column, second full paragraph.

Further, with respect to claim 36, see p. 763, first paragraph, and Fig. 6.

Further, with respect to claims 155, 156,161, the reference teaches assaying such proteins as p38 MAP kinase, and inosine-5-monophosphate dehydrogenase. p. 756, second full paragraph

Fejzo et al do not teach all the characteristics of the testing “gauges” as instantly claimed in “providing” step of claim 1. Examiner has no way of testing whether the “gauges” of Fejzo satisfy the claimed limitations. Since the Office does not have the facilities for examining and comparing applicants' gauges with the gauges of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed gauges and the gauges of the prior art.

Conclusion.

No claims are allowed

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. The examiner can normally be reached on 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael Borin, Ph.D./
Primary Examiner, Art Unit 1631

mlb